

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule comprising a polynucleotide selected from the group consisting of:

- a. a polynucleotide sequence encoding a polypeptide comprising amino acids from about 1 to about 908 in SEQ ID NO:5;
- b. a polynucleotide sequence encoding a polypeptide comprising amino acids from about 1 to about 859 in SEQ ID NO:6;
- c. a polynucleotide sequence encoding a polypeptide comprising amino acids from about 1 to about 912 in SEQ ID NO:7;
- d. a polynucleotide sequence encoding a polypeptide comprising amino acids from about 1 to about 853 in SEQ ID NO:8;
- e. a polynucleotide sequence that is at least 95% identical to the polynucleotide sequence of (a), (b), (c) or (d); and
- f. a polynucleotide sequence complementary to the polynucleotide sequence of (a), (b), (c), (d) or (e).

2. An isolated nucleic acid molecule comprising a polynucleotide selected from the group consisting of:

- a. a polynucleotide sequence at least about 20 nucleotides in length that hybridizes to the polynucleotide sequence of Claim 1(a), 1(b), 1(c), 1(d), 1(e) or 1(f) under stringent conditions; and
- b. a polynucleotide at least about 20 nucleotides in length having a nucleotide sequence complementary to any of the polynucleotide sequences in Claim 1(a), 1(b), 1(c), 1(d), 1(e) or 1(f) wherein said isolated nucleic acid molecule is not the nucleic acid molecule or nucleic acid insert identified in the following: GenBank Accession Reports: AA052791(SEQ ID NO:9); AA111043(SEQ ID NO:10); AA154890(SEQ ID NO:11); AA240794(SEQ ID NO:12); AA756653(SEQ ID NO:13); W58898(SEQ ID NO:14); W59299(SEQ ID NO:15); W91664(SEQ ID NO:16); and W91665(SEQ ID NO:17); AA116694

(SEQ ID NO:18); AA119979 (SEQ ID NO:19); AA177277 (SEQ ID NO:20); AA210568 (SEQ ID NO:21); AA399749 (SEQ ID NO:22); AA407106 (SEQ ID NO:23); and AA575617 (SEQ ID NO:24); AA004310 (SEQ ID NO:25); AA004399 (SEQ ID NO:26); AA312013 (SEQ ID NO:27); AA355824 (SEQ ID NO:28); AA533619 (SEQ ID NO:29); AA361360 (SEQ ID NO:30); AA364876 (SEQ ID NO:31); AA503090 (SEQ ID NO:32); AA533619 (SEQ ID NO:33); AA706672 (SEQ ID NO:34); AA774277 (SEQ ID NO:35); AA780277 (SEQ ID NO:36); H03349 (SEQ ID NO:37); H04031 (SEQ ID NO:38); H53133 (SEQ ID NO:39); H53239 (SEQ ID NO:40); H64669 (SEQ ID NO:41); N26002 (SEQ ID NO:42); N52936 (SEQ ID NO:43); N88352 (SEQ ID NO:44); N89594 (SEQ ID NO:45); R19795 (SEQ ID NO:46); R47511 (SEQ ID NO:47); T50235 (SEQ ID NO:48); T78023 (SEQ ID NO:49); T78186 (SEQ ID NO:50); W22886 (SEQ ID NO:51); W67657 (SEQ ID NO:52); W68094 (SEQ ID NO:53); W76111 (SEQ ID NO:54); Z38299 (SEQ ID NO:55); Z42012 (SEQ ID NO:56); G06200 (SEQ ID NO:74); AA206103 (SEQ ID NO:57); AA206264 (SEQ ID NO:58); AA216527 (SEQ ID NO:59); AA216697 (SEQ ID NO:60); AA305044 (SEQ ID NO:61); AA477705 (SEQ ID NO:62); AA477706 (SEQ ID NO:63); AA565566 (SEQ ID NO:64); AA599893 (SEQ ID NO:65); AA729418 (SEQ ID NO:66); AA887508 (SEQ ID NO:67); F09856 (SEQ ID NO:68); F12227 (SEQ ID NO:69); N39452 (SEQ ID NO:70); N48564 (SEQ ID NO:71); T66304 (SEQ ID NO:72); T66356 (SEQ ID NO:73); AA736582 (SEQ ID NO:77); AA748883 (SEQ ID NO:78); AA923295 (SEQ ID NO:79); AAI000396 (SEQ ID NO:80); AI332472 (SEQ ID NO:81); W22473 (SEQ ID NO:82); G15302 (SEQ ID NO:75) and the I.M.A.G.E. Consortium clone ID 22089 (ATCC Deposit No. 326637) (SEQ ID NO:76).

3. A method of making a recombinant vector comprising inserting an isolated nucleic acid molecule of Claim 1 into a vector selected from a group consisting of:

a. a DNA vector; and

- b. an RNA vector.
- 4. A recombinant vector comprising the isolated nucleic acid molecule of Claim 1.
 - 5. A method of making a recombinant host cell comprising introducing the recombinant vector of Claim 4 into a host cell.
 - 6. A recombinant host cell comprising the vector of Claim 4.
 - 7. A method for producing a *de novo* DNA cytosine methyltransferase polypeptide, comprising culturing the recombinant host cell of Claim 6 under conditions such that said polypeptide is expressed and recovering said polypeptide.
 - 8. An isolated nucleic acid molecule comprising polynucleotides selected from the group consisting of:
 - a. at least 50 contiguous nucleotides of SEQ ID NO:1, provided that said nucleotides are not AA052791(SEQ ID NO: 9); AA111043(SEQ ID NO:10); AA154890(SEQ ID NO:11); AA240794(SEQ ID NO:12); AA756653(SEQ ID NO:13); W58898(SEQ ID NO:14); W59299(SEQ ID NO:15); W91664(SEQ ID NO:16); W91665(SEQ ID NO:17); or any subfragment thereof; and
 - b. a nucleotide sequence complementary to a nucleotide sequence in (a).
 - 9. An isolated nucleic acid molecule comprising polynucleotides selected from the group consisting of:
 - a. at least 30 contiguous nucleotides of SEQ ID NO:2, provided that said nucleotides are not AA116694 (SEQ ID NO:18); AA119979 (SEQ ID NO:19); AA177277 (SEQ ID NO:20); AA210568 (SEQ ID NO:21); AA399749

(SEQ ID NO:22); AA407106 (SEQ ID NO:23); AA575617 (SEQ ID NO:24); or any subfragment thereof; and

b. a nucleotide sequence complementary to a nucleotide sequence in (a).

10. An isolated nucleic acid molecule comprising polynucleotides selected from the group consisting of:

a. at least 100 contiguous nucleotides of SEQ ID NO:3, provided that said nucleotides are not AA004310 (SEQ ID NO:25); AA004399 (SEQ ID NO:26); AA312013 (SEQ ID NO:27); AA355824 (SEQ ID NO:28); AA533619 (SEQ ID NO:29); AA361360 (SEQ ID NO:30); AA364876 (SEQ ID NO:31); AA503090 (SEQ ID NO:32); AA533619 (SEQ ID NO:33); AA706672 (SEQ ID NO:34); AA774277 (SEQ ID NO:35); AA780277 (SEQ ID NO:36); H03349 (SEQ ID NO:37); H04031 (SEQ ID NO:38); H53133 (SEQ ID NO:39); H53239 (SEQ ID NO:40); H64669 (SEQ ID NO:41); N26002 (SEQ ID NO:42); N52936 (SEQ ID NO:43); N88352 (SEQ ID NO:44); N89594 (SEQ ID NO:45); R19795 (SEQ ID NO:46); R47511 (SEQ ID NO:47); T50235 (SEQ ID NO:48); T78023 (SEQ ID NO:49); T78186 (SEQ ID NO:50); W22886 (SEQ ID NO:51); W67657 (SEQ ID NO:52); W68094 (SEQ ID NO:53); W76111 (SEQ ID NO:54); Z38299 (SEQ ID NO:55); Z42012 (SEQ ID NO:56); G06200 (SEQ ID NO:74); or any subfragment thereof; and

b. a nucleotide sequence complementary to a nucleotide sequence in (a).

11. An isolated polypeptide molecule comprising an amino acid sequence selected from the group consisting of:

- a. amino acids from about 1 to about 908 in SEQ ID NO:5;
- b. amino acids from about 1 to about 859 in SEQ ID NO:6;
- c. amino acids from about 1 to about 912 in SEQ ID NO:7;
- d. amino acids from about 1 to about 853 in SEQ ID NO:8; and

- e. amino acids from about 1 to about 689 in SEQ ID NO:85;
- f. amino acids from about 1 to about 689 in SEQ ID NO:86; and
- g. a polypeptide sequence at least about 90% identical to the amino acid sequence of (a), (b), (c), (d), (e) or (f).

12. An isolated polypeptide molecule, wherein except for at least one conservative amino acid substitution said polypeptide has a sequence selected from the group consisting of:

- a. amino acids from about 1 to about 908 in SEQ ID NO:5;
- b. amino acids from about 1 to about 859 in SEQ ID NO:6;
- c. amino acids from about 1 to about 912 in SEQ ID NO:7;
- d. amino acids from about 1 to about 853 in SEQ ID NO:8; and
- e. amino acids from about 1 to about 689 in SEQ ID NO:85;
- f. amino acids from about 1 to about 689 in SEQ ID NO:86; and
- g. a polypeptide sequence at least about 90% identical to the amino acid sequence of (a), (b), (c), (d), (e) or (f).

13. A method for in vitro *de novo* methylation of DNA, comprising:

- a. contacting said DNA with an effective amount of a *de novo* DNA cytosine methyltransferase polypeptide encoded by the polynucleotide of claim 1;
- b. providing an appropriately buffered solution with substrate and cofactors; and
- c. purifying said DNA.

14. A method for diagnosing or determining a susceptibility to neoplastic disorders, comprising:

- a. assaying a *de novo* DNA cytosine methyltransferase expression level in mammalian cells or body fluid; and

b. comparing said *de novo* DNA cytosine methyltransferase expression level with a standard *de novo* DNA cytosine methyltransferase expression level whereby an increase or decrease in said *de novo* DNA cytosine methyltransferase expression level over said standard is indicative of an increased or decreased susceptibility to a neoplastic disorder.

15. The method of Claim 14, wherein said *de novo* DNA cytosine methyltransferase expression level is assayed by detecting *de novo* DNA cytosine methyltransferase protein with an antibody.

16. The method of Claim 14, wherein said *de novo* DNA cytosine methyltransferase expression level is assayed by detecting *de novo* DNA cytosine methyltransferase mRNA.

17. An isolated *de novo* DNA cytosine methyltransferase polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 209933.

18. An isolated *de novo* DNA cytosine methyltransferase polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 209934.

19. An isolated *de novo* DNA cytosine methyltransferase polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 98809.

20. An isolated *de novo* DNA cytosine methyltransferase polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 326637.

21. An isolated *de novo* DNA cytosine methyltransferase Dnmt3b polypeptide wherein, except for at least one conservative amino acid substitution, said polypeptide has a sequence selected from the group consisting of:

- a. amino acid residues 1 to 362 and 383 to 859 from SEQ ID NO:2;
- and
- b. amino acid residues 1 to 362 and 383 to 749 and 813 to 859 from SEQ ID NO:2.

22. An isolated *de novo* DNA cytosine methyltransferase DNMT3B polypeptide wherein, except for at least one conservative amino acid substitution, said polypeptide has a sequence selected from the group consisting of:

- a. amino acid residues 1 to 355 and 376 to 853 from SEQ ID NO:4;
- and
- b. amino acid residues 1 to 355 and 376 to 743 and 807 to 853 from SEQ ID NO:4.

23. A method of screening for an agonist or antagonist of DNMT3A or DNMT3B DNA cytosine methyltransferase activity comprising:

- a. contacting a substrate to a DNMT3A or DNMT3B DNA cytosine methyltransferase protein or polypeptide in the presence of a putative agonist or antagonist; and
- b. assaying the activity of said agonist or said antagonist by determining at least one of the following:
 - (i) binding of said agonist or said antagonist to said DNMT3A or DNMT3B DNA cytosine methyltransferase protein or polypeptide; and
 - (ii) determining the activity of said to said DNMT3A or DNMT3B DNA cytosine methyltransferase protein or polypeptide in the presence of said agonist or said antagonist.

24. The nucleic acid molecule of claim 1, wherein said polynucleotide encodes a polypeptide capable of methylation at the C5 position of cytosine in DNA.

25. The nucleic acid molecule of claim 1, wherein said polynucleotide is that of part (a).

26. The nucleic acid molecule of claim 1, wherein said polynucleotide is that of part (b).

27. The nucleic acid molecule of claim 1, wherein said polynucleotide is that of part (c).

28. The nucleic acid molecule of claim 1, wherein said polynucleotide is that of part (d).

29. The nucleic acid molecule of claim 1, wherein said polynucleotide is that of part (e).

30. The nucleic acid molecule of claim 1, wherein said polynucleotide is that of part (f).

31. An isolated nucleic acid molecule comprising a polynucleotide selected from the group consisting of:

a. a polynucleotide sequence encoding mouse Dnmt3a polypeptide contained in ATCC Deposit No. 209933;

b. a polynucleotide sequence encoding mouse Dnmt3b polypeptide contained in ATCC Deposit No. 209934;

c. a polynucleotide sequence encoding human DNMT3A polypeptide contained in ATCC Deposit No. 98809;

d. a polynucleotide sequence encoding human DNMT3B polypeptide contained in ATCC Deposit No. 326637;

e. a polynucleotide sequence at least 95% identical to the polynucleotide sequence of (a), (b), (c) or (d); and

f. a polynucleotide sequence complementary to the polynucleotide sequence of (a), (b), (c), (d) or (e).

32. The nucleic acid molecule of claim 31, wherein said polynucleotide is that of part (a).

33. The nucleic acid molecule of claim 31, wherein said polynucleotide is that of part (b).

34. The nucleic acid molecule of claim 31, wherein said polynucleotide is that of part (c).

35. The nucleic acid molecule of claim 31, wherein said polynucleotide is that of part (d).

36. The nucleic acid molecule of claim 31, wherein said polynucleotide is that of part (e).

37. The nucleic acid molecule of claim 31, wherein said polynucleotide is that of part (f).

38. An isolated nucleic acid molecule comprising a polynucleotide selected from the group consisting of:

a. a polynucleotide sequence encoding a polypeptide comprising amino acids from about 1 to about 689 in SEQ ID NO:85;

- b. a polynucleotide sequence encoding a polypeptide comprising amino acids from about 1 to about 689 in SEQ ID NO:86;
- c. a polynucleotide sequence that is at least 95% identical to the polynucleotide sequence of (a) or (b); and
- d. a polynucleotide sequence complementary to the polynucleotide sequence of (a), (b) or (c).

39. The nucleic acid molecule of claim 38, wherein said polynucleotide is that of part (a).

40. The nucleic acid molecule of claim 38, wherein said polynucleotide is that of part (b).

41. The nucleic acid molecule of claim 38, wherein said polynucleotide is that of part (c).

42. The nucleic acid molecule of claim 38, wherein said polynucleotide is that of part (d).

43. An isolated *de novo* DNA cytosine methyltransferase polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-4611.

44. An isolated *de novo* DNA cytosine methyltransferase polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-4610.

45. A method of making a recombinant vector comprising inserting an isolated nucleic acid molecule of Claim 38 into a vector selected from a group consisting of:

- a. a DNA vector; and
 - b. an RNA vector.
46. A recombinant vector comprising the isolated nucleic acid molecule of Claim 38.
47. A method of making a recombinant host cell comprising introducing the recombinant vector of Claim 46 into a host cell.
48. A recombinant host cell comprising the vector of Claim 46.
49. A method for producing a *de novo* DNA cytosine methyltransferase polypeptide, comprising culturing the recombinant host cell of Claim 48 under conditions such that said polypeptide is expressed and recovering said polypeptide.
50. A method for in vitro *de novo* methylation of DNA, comprising:
- a. contacting said DNA with an effective amount of a *de novo* DNA cytosine methyltransferase polypeptide encoded by the polynucleotide of claim 38;
 - b. providing an appropriately buffered solution with substrate and cofactors; and
 - c. purifying said DNA.
51. An isolated nucleic acid molecule comprising a polynucleotide selected from the group consisting of:
- a. a polynucleotide sequence encoding mouse Dnmt3a2 polypeptide contained in ATCC Deposit No. PTA-4611;
 - b. a polynucleotide sequence encoding human DNMT3A2 polypeptide contained in ATCC Deposit No. PTA-4610;

c. a polynucleotide sequence at least 95% identical to the polynucleotide sequence of (a) or (b); and

d. a polynucleotide sequence complementary to the polynucleotide sequence of (a), (b) or (c).

52. The nucleic acid molecule of claim 51, wherein said polynucleotide is that of part (a).

53. The nucleic acid molecule of claim 51, wherein said polynucleotide is that of part (b).

54. The nucleic acid molecule of claim 51, wherein said polynucleotide is that of part (c).

55. The nucleic acid molecule of claim 51, wherein said polynucleotide is that of part (d).